IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:	)	Art Unit: 1647
Nielsen, et al.	)	Examiner: Deberry, R.
Serial No: 09/674,733	)	Washington, D.C.
Filed: May 2, 2001	)	
For: METHODS FOR TREATMENT OF DISEASES ASSOCIATED WITH INFLAMMATION UNDER NON-ISCHEMIC CONDITIONS	)	Docket No.: Nielsen=3B Confirmation No.: 3818

DECLARATION OF ELSE TØNNESEN

U.S. Patent and Trademark Office
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Alexandria, VA 22314

I hereby state and declare as follows:

1. I am a Professor and chief physician at the Department of Anaestesiology and Critical Care at Aarhus University Hospital, Denmark.
2. I am a person skilled in the fields of anaestesiology, critical care- and pulmonary medicine which with all respect appears from my CV (attached).
3. I am working with clinical and experimental studies to obtain an in depth understanding of the pathophysiological mechanisms responsible for organ damage in critically ill patients. We are currently conducting a series of studies using LPS induced inflammation in pigs to define the role of various cytokines (TNF-alpha, IL6 and IL10) for the inflammatory response seen in these conditions. Importantly, these studies have demonstrated that it is possible to interfere with the plasma concentrations of cytokines and protect against organ damage including the lungs.
4. I have read the Office Action dated December 14, 2004 and can assure you that experimentally inhalation of LPS is a widely recognized model for exacerbations of chronic obstructive pulmonary disease (COPD).
5. COPD is a chronic progressive disease associated with exacerbations. An exacerbation is defined as an acute worsening of a condition. Thus associated with COPD, an exacerbation can be defined clinically as a complex of respiratory symptoms (i.e. new onset or worsening of more

than one symptom such as cough, sputum, dyspnea or wheeze) lasting for at least 3 days, the exacerbation in COPD being characterized by eosinophilic and neutrophilic lung inflammation.

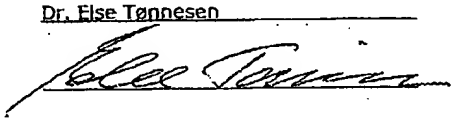
Experimentally, inhalation of lipopolysaccharide (LPS) induces an inflammatory response with eosinophil and neutrophil infiltrations that mimics the inflammatory response seen during an exacerbation in COPD.

For this reason, the model of acute lung inflammation induced by LPS inhalation is a used model to study exacerbations in COPD.

6. To emphasize the wide spread application of the LPS inhalation as a model for exacerbations in COPD, we have attached a list of references wherein the model is applied.
7. In addition to the general understanding that LPS inhalation is a recognized model for exacerbations in COPD, this approach is also valuable for proteomic studies identifying the pathogenic pathways involved in the progression of COPD.
8. Examples of practical applications of the model has been highlighted in several scientific publications (Brigham and Meyrick, Am Rev Respir Dis. 133:913-27, 1986; Wagner et al., Am J Respir Cell Mol Biol 20:769–776, 1999; Arsalane et al., Am J Respir Crit Care Med 161:1624–1630, 2000; Ridger et al., J Immunol 166:3484-90, 2001).
9. Conclusively, it is without no doubt that exacerbations in COPD occur commonly and are characterized by an inflammatory pattern including the release of several cytokines and cell adhesion molecules enhancing the mainly bronchial neutrophilic inflammation. Importantly, LPS inhalation is a recognized model to examine the effect of exacerbations in COPD.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: June 13, 2005 By: Dr. Else Tønnesen



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CURRICULUM VITAE

Personal data

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1968	Advanced level in mathematics and physics
1975	Doctor of Medicine, MD, University of Aarhus
1984-87	Clinical assistant, University Hospital of Odense
1988	Authorised as Specialist in Anaesthesiology after education in Sweden (Falköping and Malmö), Esbjerg Centralsygehus and University Hospital of Odense
1992-95	Consultant and lecturer at Dept. of Anaesthesiology and Intensive Care, University Hospital of Odense
1993-95	Vice Rector of the University of Southern Denmark
01.09.95-	Professor and Consultant, Department of Anaesthesiology and Intensive Care, Aarhus University Hospital
01.02.02-	Vice Dean at the Faculty of Health Sciences, University of Aarhus

Research activities

DMSc in 1989 from University of Southern Denmark with the dissertation *"Immunological aspects of anaesthesia. With special reference to NK cells"*. Has published approximately 100 original papers and reviews in addition to case reports and other publications. Eight book chapters. Three chapters in textbooks editorial process. More than 150 speeches/poster presentations and approximately 35 guest lectures.

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